

Claims

1. Use of a nucleotide sequence derived from all or part of the 5' end of the genomic RNA of a type C retrovirus with the exception of the Friend (FMLV) and Moloney (MoMLV) murine leukemia viruses, as internal ribosome entry site (IRES) in a vector and/or for allowing or improving the encapsidation of a retroviral vector.
2. Use according to claim 1, according to which the type C retrovirus is selected from the REV, MSV, MHV, MEV, FMOV, AMLV, MEELV, SFFV, RASV, FLV, FSV, EFLV, SSV, GALV and BAEV viruses.
3. Use according to claim 2, according to which said nucleotide sequence is derived from all or part of the 5' end of the genomic RNA of a reticuloendotheliosis virus.
4. Use according to claim 3, according to which said nucleotide sequence is derived from all or part of the 5' end of the genomic RNA of an avian reticuloendotheliosis virus and in particular type A.
5. Use according to ^{claim 1} ~~one of claims 1 to 4~~, according to which said nucleotide sequence is substantially homologous or identical to all or part of the sequence presented in the sequence identifier SEQ ID NO: 1.
6. Use according to claim 5, according to which said nucleotide sequence is substantially homologous or identical to the sequence presented in the sequence identifier SEQ ID NO: 2:
- (i) starting at nucleotide 1 and ending at nucleotide 578,
 - (ii) starting at nucleotide 265 and ending at nucleotide 578, or
 - (iii) starting at nucleotide 452 and ending at nucleotide 578.
7. Use according to claim 6, according to which said nucleotide sequence is identical to the sequence presented in the sequence identifier SEQ ID NO: 2:

(i) starting at nucleotide 1 and ending at nucleotide 578,

(ii) starting at nucleotide 265 and ending at nucleotide 578, or

5 (iii) starting at nucleotide 452 and ending at nucleotide 578.

Sub c'
a 8. Vector for the expression of one or more genes of interest comprising said nucleotide sequence used according to ^{claim 1} ~~one of claims 1 to 7~~.

10 9. Vector according to claim 8, characterized in that it is a plasmid vector or a viral vector derived from a virus selected from the poxvirus, adenovirus, baculovirus, herpesvirus, adeno-associated virus and retrovirus group.

Sub b' 7
15 10. Vector according to claim 8 or 9, which is derived from a retrovirus and which comprises at least the following elements associated in a functional manner: a retroviral 5' LTR and a retroviral 3' LTR, one or more genes of interest, and said nucleotide
20 sequence as defined in one of claims 1 to 7 to allow or improve the encapsidation of said vector into a viral particle and/or as an IRES site to allow or promote the expression of a gene of interest positioned downstream of said nucleotide sequence.

25 11. Retroviral vector according to claim 10, in which said nucleotide sequence is as an IRES site and comprising, in addition, an encapsidation region which is heterologous to said nucleotide sequence.

a 12. Retroviral vector according to claim 10 ~~or 11~~,
30 comprising at least:

- (a) a retroviral 5' LTR,
- (b) an encapsidation region,
- (c) optionally, a first gene of interest followed by an internal promoter region a different origin
35 from that of said retroviral 5' LTR,
- (d) a second gene of interest,
- (e) an IRES site,
- (f) a third gene of interest, and
- (g) a retroviral 3' LTR,

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at least one of the encapsidation region and the IRES site consisting of said nucleotide sequence ~~used according to one of claims 1 to 7.~~

13. Retroviral vector according to claim 12, in which the internal promoter region, the second gene of interest, the IRES site and the third gene of interest are in an opposite orientation relative to the retroviral 5' and 3' LTRs.

Sub 7
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C1
10 14. Retroviral vector according to claim 12 or 13, in which the encapsidation region is derived from a murine retrovirus, especially from an MoMLV, or from a VL30-type retrotransposon and the IRES site comprises a nucleotide sequence as defined in claim 6.

15 15. Retroviral vector according to claim 14, in which the encapsidation region is derived from an MoMLV and the IRES site comprises a nucleotide sequence identical to the sequence presented in sequence identifier SEQ ID NO: 2 starting at nucleotide 265 and ending at nucleotide 578 or starting at nucleotide 452 and ending at nucleotide 578.

16. Retroviral vector according to claim 10, comprising a retroviral 5' LTR derived from an REV virus, especially SNV, a retroviral 3' LTR of any origin, one or more genes of interest, and a nucleotide sequence which is substantially homologous or identical to the sequence presented in the sequence identifier SEQ ID NO: 2 starting at nucleotide 1 and ending at nucleotide 578, or starting at nucleotide 265 and ending at nucleotide 578, as encapsidation region.

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17. Vector according to ^{claim 8} ~~one of claims 8 to 16~~, comprising a gene of interest encoding a product of expression selected from factor VIII, factor IX, the CFTR protein, dystrophin, insulin, alpha-, beta- or gamma-interferon, an interleukin (IL) especially IL-2 and a selectable marker.

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18. Viral particle generated from a viral vector according to ^{claim 8} ~~one of claims 8 to 17.~~

19. Cell comprising a vector according to one of claims 8 to 17 or infected with a viral particle according to claim 18.

20. Use of a vector according to one of claims 8 to 17, of a viral particle according to claim 18 or of a cell according to claim 19 for the preparation of a pharmaceutical composition intended for the treatment and/or for the prevention of a disease which is treatable by gene therapy.

10 21. Use of a vector according to one of claims 8 to
17, of a viral particle according to claim 18 or of a
cell according to claim 19 for the preparation of one
or more polypeptides of interest by the recombinant
route or for the protection of a transgenic animal.

15 22. Pharmaceutical composition comprising, as
therapeutic or prophylactic agent, a vector according
to one of claims 8 to 17, a viral particle according to
claim 18, a cell according to claim 19 or a polypeptide
of interest obtained according to the use according to
20 claim 21, in combination with a pharmaceutically
acceptable vehicle.

C² 23. Pharmaceutical composition according to claim 22, characterized in that it comprises between 10^4 and 10^{14} pfu, and preferably between 10^6 and 10^{11} pfu viral particles according to claim 18.

24. Use of a vector according to one of claims 8 to 17, of a viral particle according to claim 18 or of a pharmaceutical composition according to claim 22 or 23, for the transfection or infection of pluripotent cells, especially pluripotent cells of the central nervous system.

add c^3
add D^{15}